

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	311	(myxococcus adj xanthus) OR ("M." adj xanthus)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:30
L2	12	11 same bacteriophage	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:33
L3	19	11 same integrase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:31
L4	42	mx9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:33
L5	13	11 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:35
L6	2008	epothilone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:35
L7	54	11 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:35
L8	11	l4 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:41
L9	9	l4 same l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/02 11:41
S1	1	("6833447").PN.	USPAT	OR	OFF	2006/02/02 11:29
S2	1	("6303342").PN.	USPAT	OR	OFF	2006/02/01 21:52
S3	19	bryan near2 julien.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/01 21:57
S4	42	mx9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/02/01 21:57

FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 12:34:20 ON 02 FEB 2006

L1 3660 S (MYXOCOCCUS XANTHUS) OR (M. XANTHUS)  
L2 85 S L1 (P) BACTERIOPHAGE  
L3 7 S L1 (P) MX9  
L4 5 S MX9 (P) INTEGRASE  
L5 40 S L1 (P) EPOTHILONE  
L6 7 S MX9 (P) ((BACTERIOPHAGE) OR (PHAGE))  
L7 3 DUP REM L3 (4 DUPLICATES REMOVED)  
L8 32 DUP REM L2 (53 DUPLICATES REMOVED)  
L9 2 S L8 AND MX9  
L10 2 DUP REM L4 (3 DUPLICATES REMOVED)  
L11 1 S L5 AND MX9  
L12 3 DUP REM L6 (4 DUPLICATES REMOVED)  
L13 19 DUP REM L5 (21 DUPLICATES REMOVED)  
L14 1 S L13 AND (PHAGE OR BACTERIOPHAGE)

Martin, Sandra; Sodergren, Erica; Masuda, Terrie; Kaiser, Dale

SO Virology (1978), 88(1), 44-53  
CODEN: VIRLAX; ISSN: 0042-6822

TI Systematic isolation of transducing phages for *Myxococcus xanthus*

AB Six new phages active on *M. xanthus* were isolated from cultures of myxobacteria. The 6 are capable of transduction, and fall into 3 groups. Members of 1 group have long contractile tails, have a characteristic neutralization antigen, and resembled the previously described Mx4. Members of a 2nd group, exemplified by Mx8, had very short tails and a characteristic antigen. Mx9, the sole member of the 3rd group, has a very short tail and a characteristic antigen. Phage Mx8, which is active on fruiting as well as nonfruiting strains of *M. xanthus*, transduced auxotrophic, antibiotic resistance, and motility markers in *M. xanthus*. Although crude lysates of Mx8 contained 58-nm diam. particles with a tail and 29-nm particles without tail, only 58-nm particles could form plaques and transduce. The plaque-forming particles of Mx8 possessed a single DNA molecule of 56,000 base pairs with a buoyant d. of 1.726 g/cm<sup>3</sup>, virtually identical to that of the DNA from its host.

Julien Bryan

SO Journal of bacteriology, (2003 Nov) 185 (21) 6325-30.  
Journal code: 2985120R. ISSN: 0021-9193.

TI Characterization of the integrase gene and attachment site for the *Myxococcus xanthus* bacteriophage Mx9.

AB Bacteriophage Mx9 is a temperate phage that infects *Myxococcus xanthus*. It lysogenizes the bacteria by integrating into the bacterial chromosome by site-specific recombination at one of two sites, attB1 or attB2. Integration at attB1 results in deletion of DNA between the two attB sites. The attB2 site lies within the 5' region of the *M. xanthus* tRNA(Gly) gene. Mx9 integration requires a single protein, Int. Analysis of integration revealed that the phage attachment site (attP) is contained in the int gene and that upon integration, the 3' end of the int gene is altered. Plasmids containing fusions of the pilA or mgl promoter to lacZ integrated at either Mx9 attB site have higher levels of transcription than the same fusions integrated at the Mx8 attB site

IN Julien, Bryan.

SO PCT Int. Appl., 37 pp.  
CODEN: PIXXD2

TI Transformation system based on the integrase gene and attachment site for *Myxococcus xanthus* bacteriophage Mx9

AB The invention provides a transformation system based on bacteriophage Mx9, a temperate phage that infects *Myxococcus xanthus*. Mx9 lysogenizes the bacteria by integrating

into the bacterial chromosome by site-specific recombination at one of two sites, attB1 or attB2. Mx9 integration requires a single protein, integrase encoded by int gene. Integration at attB1 results in deletion of DNA between the two attB sites. The attB2 site lies within the 5' region of the *M. xanthus* tRNAGly gene. Anal. of integration revealed that the phage attachment site (attP) is contained in the int gene and that upon integration, the 3' end of the int gene is altered. Plasmids contg. fusions of the pilA or mgl promoter to lacZ integrated at either Mx9 attB site have higher levels of transcription than the same fusions integrated at the Mx8 attB site. Specifically disclosed and claimed are Mx9 integrase gene and attB2 integration site. Vectors contg. an integrase encoding gene and a phage attachment site (attP) integrate into a chromosomal attB site and can be used to alter or introduce genes into a variety of host cells.

- AU Lau Janice; Frykman Scott; Regentin Rika; Ou Sally; Tsuruta Hiroko; Licari Peter  
SO Biotechnology and bioengineering, (2002 May 5) 78 (3) 280-8.  
Journal code: 7502021. ISSN: 0006-3592.  
TI Optimizing the heterologous production of epothilone D in *Myxococcus xanthus*.  
AB The heterologous production of epothilone D in *Myxococcus xanthus* was improved by 140-fold from an initial titer of 0.16 mg/L with the incorporation of an adsorber resin, the identification of a suitable carbon source, and the implementation of a fed-batch process. To reduce the degradation of epothilone D in the basal medium, XAD-16 (20 g/L) was added to stabilize the secreted product. This greatly facilitated its recovery and enhanced the yield by three-fold. The potential of using oils as a carbon source for cell growth and product formation was also evaluated. From a screen of various oils, methyl oleate was shown to have the greatest impact. At the optimal concentration of 7 mL/L in a batch process, the maximum cell density was increased from 0.4 g dry cell weight (DCW)/L to 2 g DCW/L. Product yield, however, depended on the presence of trace elements in the production medium. With an exogenous supplement of trace metals to the basal medium, the peak epothilone D titer was enhanced eight-fold. This finding demonstrates the significant role of metal ions in cell metabolism and in epothilone biosynthesis. To further increase the product yield, a continuous fed-batch process was used to promote a higher cell density and to maintain an extended production period. The optimized fed-batch cultures consistently yielded a cell density of 7 g DCW/L and an average production titer of 23 mg/L.
- AU Julien Bryan; Shah Sanjay  
SO Antimicrobial agents and chemotherapy, (2002 Sep) 46 (9) 2772-8.  
Journal code: 0315061. ISSN: 0066-4804.  
TI Heterologous expression of epothilone biosynthetic genes in *Myxococcus xanthus*.  
AB Epothilones are potential anticancer drugs that stabilize microtubules in a manner similar to paclitaxel (Taxol). Epothilones are produced from the myxobacterium *Sorangium cellulosum*, which has a 16-h doubling time and produces only milligram-per-liter amounts of epothilone A and epothilone B. Furthermore, genetic manipulation of *S. cellulosum* is difficult. To produce epothilones in a more genetically amenable and rapidly growing host, we chose the closely related and best-characterized myxobacteria *Myxococcus xanthus*. We inserted 65.4 kb of *S. cellulosum* DNA that encompassed the entire epothilone gene cluster into the chromosome of *M. xanthus* by a series of homologous recombination events. The resulting strain produced epothilones A and B. Construction of a strain that contained a mutation in epoK, the P450 epoxidase, resulted in production of epothilones C and D.

AU Gerth Klaus; Pradella Silke; Perlova Olena; Beyer Stefan; Muller Rolf  
SO Journal of biotechnology, (2003 Dec 19) 106 (2-3) 233-53. Ref: 90  
Journal code: 8411927. ISSN: 0168-1656.

TI Myxobacteria: proficient producers of novel natural products with various biological activities--past and future biotechnological aspects with the focus on the genus *Sorangium*.

AB Myxobacteria are gram-negative bacteria which are most noted for their ability to form fruiting bodies upon starvation. Within the last two decades, they increasingly gained attention as producers of natural products with biological activity. Here, recent and future biotechnological research on certain key myxobacteria and on their ability to produce natural products is reviewed with the focus on the production of myxovirescin, soraphen and epothilone. Aspects of product improvement and yield as well as statistics regarding secondary metabolite formation are discussed. Future research will deal with the exploitation of the biosynthetic potential of the myxobacteria, for example via the isolation of new myxobacterial species with different physiological properties. Additionally, the genetic potential of myxobacteria to form natural products can be exploited by the identification and activation of biosynthetic gene clusters. These can be found frequently within their genomes, which is shown by the analysis of the unfinished genomes of *Myxococcus xanthus* and *Sorangium cellulosum*. The current status of the *S. cellulosum* functional genome project with model strain So ce56 is discussed.